201-15345

HPV Program

Data Set

Existing Chemical	:	ID: 68551-11-1
Memo	:	A complex combination of products produced by the distillation of products from the hydrogenation of butanal from the hydroformylation of propene. It consists predominantly of organic compounds such as aldehydes, alcohols, esters, ethers a
CAS No.	:	68551-11-1
EINECS Name	:	1-Propene, hydroformylation products, high-boiling
EC No.	:	271-363-2
TSCA Name	:	1-Propene, hydroformylation products, high-boiling

Producer related part

Company	:	BASF Corporation
Creation date	:	29.12.2003
Status	:	
Memo	:	Prepared by: Toxicology and Regulatory Affairs Freeburg IL 62243 rauckman@toxicsolutions.com
Printing date	:	07.06.2004
Revision date	:	
Date of last update	:	07.06.2004
Number of pages	:	30
Chapter (profile)	:	Chapter: 1.0.1, 1.2, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6.1, 3.1.1, 3.1.2, 3.3.1, 3.3.2, 3.5, 4.1, 4.2, 4.3, 4.4, 5.1.1, 5.1.2, 5.1.3, 5.1.4, 5.4, 5.5, 5.6, 5.7, 5.8.1, 5.8.2
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

2.1 MELTING POINT

Value : ca. -90 °C

Method :
This value is approximate and was derived experimentally at the manufacturing plant using a standard method.

Remark :
As this material is a variable mixture this must be considered as only an approximation of the actual freezing point for any batch.

Test substance :
EP-202 (CASNO 68551-11-1)

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
02.01.2004

2.2 BOILING POINT

Value : ca. 155 - 250 °C at 1013 hPa

Method :
This value is approximate and was derived experimentally at the manufacturing plant using a standard method.

Remark :
As this material is a variable mixture this must be considered as only an approximation of the boiling point for any batch.

Test substance :
EP-202 (CASNO 68551-11-1)

Reliability : (2) valid with restrictions
Flag : Critical study for SIDS endpoint
02.01.2004

2.4 VAPOUR PRESSURE

Value : ca. 1.3 hPa at 25 °C
Decomposition :
Method : other (calculated)
Year :
GLP :
Test substance :

Method :
The vapor pressure for the mixture is estimated using the mean of the Antoine & Grain methods as calculated using the MPBPWIN v1.40 program found in EPIWIN 3.05. The initial boiling point and the final boiling point are the only input parameters this estimate is based upon, as the program is insensitive to structure, using a determined boiling point as an input provides an estimate of the VP. Likewise the program is insensitive to melting point when calculating VPs for liquids.

The structure for 2-ethylhexanol was entered to provide a reference value

for one of the pure major components.

As this is a variable mixture, the initial and final boiling point values are also variable.

Result :

Experimental Database Structure Match:
Name : 2-ETHYL-1-HEXANOL
CAS Num : 000104-76-7
Exp MP (deg C): -70
Exp BP (deg C): 184.6
Exp VP (mm Hg): 1.36E-01
Exp VP (deg C): 25
Exp VP ref : DAUBERT,TE & DANNER,RP (1985)

SMILES : CCCCC(CC)CO
CHEM : EP-202
MOL FOR: C8 H18 O1
MOL WT : 130.23

+++++++BASED ON INITIAL BP OF 155 deg C

---------- SUMMARY MPBPWIN v1.40 ----------

Boiling Point: 188.52 deg C (Adapted Stein and Brown Method)

Melting Point: -47.42 deg C (Adapted Joback Method)
Melting Point: -3.59 deg C (Gold and Ogle Method)
Mean Melt Pt : -25.50 deg C (Joback; Gold,Ogle Methods)
Selected MP: -25.50 deg C (Mean Value)

Vapor Pressure Estimations (25 deg C):
(Using BP: 155.00 deg C (user entered))
(MP not used for liquids)
VP: 1.13 mm Hg (Antoine Method)
VP: 0.912 mm Hg (Modified Grain Method)
VP: 4.26 mm Hg (Mackay Method)
Selected VP: 1.02 mm Hg (Mean of Antoine & Grain methods)

+++++++++ BASED ON FINAL BP OF 250 dec C
---------- SUMMARY MPBPWIN v1.40 ----------
Boiling Point: 188.52 deg C (Adapted Stein and Brown Method)

Melting Point: -47.42 deg C (Adapted Joback Method)
Melting Point: -3.59 deg C (Gold and Ogle Method)
Mean Melt Pt : -25.50 deg C (Joback; Gold,Ogle Methods)
Selected MP: -25.50 deg C (Mean Value)

Vapor Pressure Estimations (25 deg C):
(Using BP: 250.00 deg C (user entered))
(MP not used for liquids)
VP: 0.00334 mm Hg (Antoine Method)
VP: 0.00316 mm Hg (Modified Grain Method)
VP: 0.047 mm Hg (Mackay Method)
Selected VP: 0.00325 mm Hg (Mean of Antoine & Grain methods)

Test substance :

EP-202 (CASNO 68551-11-1)

Conclusion

The calculated vapor pressure for this mixture, assuming it is a pure material of boiling point 122 deg C, is approximately 1 mm Hg. As this is a variable mixture, a specific VP cannot be stated. It is concluded that giving the VP as a range of 1 to 5 hPa is a conservative, yet realistic estimate.

Reliability : (2) valid with restrictions

Estimates using an acceptable method are assigned a reliability score of 2.

Flag : Critical study for SIDS endpoint

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2.5 PARTITION COEFFICIENT

Partition coefficient : octanol-water
Log pow : at °C
pH value :

Method : Octanol water partition coefficients for the major components of EP-202 were obtained through the KOWWIN program (v1.66) by entering the structure of the component into the program using the SMILES code. These codes are listed in the results section. Where there was an experimental value found in the database associated with the program, that value was accepted. Where an experimental value was not found the program estimate was accepted.

Result :

```
KOWWIN Program (v1.66) Results:
==============================

SMILES : CCCC=C(CC)C=O
CHEM   : 2-Ethylhexenal
MOL FOR: C8 H14 O1
MOL WT : 126.20
Log Kow(version 1.66 estimate): 2.62

-------+-----+-----------------------------------------+---------+--------
 TYPE  | NUM |        LOGKOW FRAGMENT DESCRIPTION      |  COEFF  |  VALUE
-------+-----+-----------------------------------------+---------+--------
 Frag  |  2  |  -CH3    [aliphatic carbon]             | 0.5473  |  1.0946
 Frag  |  3  |  -CH2-   [aliphatic carbon]             | 0.4911  |  1.4733
 Frag  |  2  |  =CH- or =C<  [olefinc carbon]          | 0.3836  |  0.7672
 Frag  |  1  |  -CHO    [aldehyde, aliphatic attach]   |-0.9422  | -0.9422
 Const |     |  Equation Constant                      |         |  0.2290
-------+-----+-----------------------------------------+---------+--------
                                                      Log Kow   =   2.6219


SMILES : CCCCC(CC)C=O
CHEM   : 2-Ethylhexanal
MOL FOR: C8 H16 O1
MOL WT : 128.22
Log Kow(version 1.66 estimate): 2.71

-------+-----+-----------------------------------------+---------+--------
 TYPE  | NUM |        LOGKOW FRAGMENT DESCRIPTION      |  COEFF  |  VALUE
-------+-----+-----------------------------------------+---------+--------
 Frag  |  2  |  -CH3    [aliphatic carbon]             | 0.5473  |  1.0946
 Frag  |  4  |  -CH2-   [aliphatic carbon]             | 0.4911  |  1.9644
 Frag  |  1  |  -CH     [aliphatic carbon]             | 0.3614  |  0.3614
 Frag  |  1  |  -CHO    [aldehyde, aliphatic attach]   |-0.9422  | -0.9422
 Const |     |  Equation Constant                      |         |  0.2290
-------+-----+-----------------------------------------+---------+--------
                                                      Log Kow   =   2.7072
```

SMILES : CCCCO
CHEM : n-Butanol
MOL FOR: C4 H10 O1
MOL WT : 74.12
Log Kow(version 1.66 estimate): 0.84

Experimental Database Structure Match:
Name : 1-Butanol
CAS Num : 000071-36-3
Exp Log P: 0.88
Exp Ref : Hansch,C et al. (1995)

TYPE	NUM	LOGKOW FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	1	-CH3 [aliphatic carbon]	0.5473	0.5473
Frag	3	-CH2- [aliphatic carbon]	0.4911	1.4733
Frag	1	-OH [hydroxy, aliphatic attach]	-1.4086	-1.4086
Const		Equation Constant		0.2290
			Log Kow =	0.8410

SMILES : CCCC(O)C(CC)CO
CHEM : 2-Ethyl-1,3-hexanediol
MOL FOR: C8 H18 O2
MOL WT : 146.23
Log Kow(version 1.66 estimate): 1.60

TYPE	NUM	LOGKOW FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	2	-CH3 [aliphatic carbon]	0.5473	1.0946
Frag	4	-CH2- [aliphatic carbon]	0.4911	1.9644
Frag	2	-CH [aliphatic carbon]	0.3614	0.7228
Frag	2	-OH [hydroxy, aliphatic attach]	-1.4086	-2.8172
Factor	1	Multi-alcohol correction	0.4064	0.4064
Const		Equation Constant		0.2290
			Log Kow =	1.6000

SMILES : CCCC(OC(=O)CCC)C(CC)COC(=O)CCC
CHEM : 2-Ethylhexyl-1,3-dibutyrate
MOL FOR: C16 H30 O4
MOL WT : 286.42
Log Kow(version 1.66 estimate): 5.17

TYPE	NUM	LOGKOW FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	4	-CH3 [aliphatic carbon]	0.5473	2.1892
Frag	8	-CH2- [aliphatic carbon]	0.4911	3.9288
Frag	2	-CH [aliphatic carbon]	0.3614	0.7228
Frag	2	-C(=O)O [ester, aliphatic attach]	-0.9505	-1.9010
Const		Equation Constant		0.2290
			Log Kow =	5.1688

SMILES : CCCC(=O)OCCCC
CHEM : N-butyl-n-butyrate
MOL FOR: C8 H16 O2
MOL WT : 144.22
Log Kow(version 1.66 estimate): 2.83

TYPE	NUM	LOGKOW FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	2	-CH3 [aliphatic carbon]	0.5473	1.0946
Frag	5	-CH2- [aliphatic carbon]	0.4911	2.4555
Frag	1	-C(=O)O [ester, aliphatic attach]	-0.9505	-0.9505
Const		Equation Constant		0.2290
			Log Kow =	2.8286

```
SMILES : CCCC=O
CHEM   : N-butyraldehyde
MOL FOR: C4 H8 O1
MOL WT : 72.11
Log Kow(version 1.66 estimate): 0.82

Experimental Database Structure Match:
  Name     :  Butyraldehyde
  CAS Num  :  000123-72-8
  Exp Log P:  0.88
  Exp Ref  :  Hansch,C et al. (1995)

-------+-----+-------------------------------------------+---------+--------
 TYPE  | NUM |        LOGKOW FRAGMENT DESCRIPTION        |  COEFF  |  VALUE
-------+-----+-------------------------------------------+---------+--------
 Frag  |  1  |  -CH3    [aliphatic carbon]               | 0.5473  |  0.5473
 Frag  |  2  |  -CH2-   [aliphatic carbon]               | 0.4911  |  0.9822
 Frag  |  1  |  -CHO    [aldehyde, aliphatic attach]     |-0.9422  | -0.9422
 Const |     |  Equation Constant                        |         |  0.2290
-------+-----+-------------------------------------------+---------+--------
                                                        Log Kow   =   0.8163

SMILES : C1(CCC)C(CC)COC(CCC)O1
CHEM   : 2,4-Dipropyl-5-ethyl-1,3-dioxane
MOL FOR: C12 H24 O2
MOL WT : 200.32
Log Kow(version 1.66 estimate): 3.89

-------+-----+-------------------------------------------+---------+--------
 TYPE  | NUM |        LOGKOW FRAGMENT DESCRIPTION        |  COEFF  |  VALUE
-------+-----+-------------------------------------------+---------+--------
 Frag  |  3  |  -CH3    [aliphatic carbon]               | 0.5473  |  1.6419
 Frag  |  6  |  -CH2-   [aliphatic carbon]               | 0.4911  |  2.9466
 Frag  |  3  |  -CH     [aliphatic carbon]               | 0.3614  |  1.0842
 Frag  |  2  |  -O-     [oxygen, aliphatic attach]       |-1.2566  | -2.5132
 Factor|  1  |  C-O-C-O-C  structure  correction         | 0.5036  |  0.5036
 Const |     |  Equation Constant                        |         |  0.2290
-------+-----+-------------------------------------------+---------+--------
                                                         Log Kow   =   3.8921

SMILES : CCCCC(CC)CO
CHEM   : 2-Ethylhexanol
MOL FOR: C8 H18 O1
MOL WT : 130.23
Log Kow(version 1.66 estimate): 2.73

-------+-----+-------------------------------------------+---------+--------
 TYPE  | NUM |        LOGKOW FRAGMENT DESCRIPTION        |  COEFF  |  VALUE
-------+-----+-------------------------------------------+---------+--------
 Frag  |  2  |  -CH3    [aliphatic carbon]               | 0.5473  |  1.0946
 Frag  |  5  |  -CH2-   [aliphatic carbon]               | 0.4911  |  2.4555
 Frag  |  1  |  -CH     [aliphatic carbon]               | 0.3614  |  0.3614
 Frag  |  1  |  -OH     [hydroxy, aliphatic attach]      |-1.4086  | -1.4086
 Const |     |  Equation Constant                        |         |  0.2290
-------+-----+-------------------------------------------+---------+--------
                                                        Log Kow   =   2.7319
```

Test substance : Components of EP-202

Conclusion : The following values were found for log Kow

COMPONENT********	**log Kow**	
2-Ethylhexenal	2.62	c
2-Ethylhexanal	2.71	c
N-butanol	0.88	e
2-Ethyl-1,3-hexanediol	1.60	c
2-Ethylhexyl-1,3-dibutyrate	5.17	c
N-butyl-n-butyrate	2.83	c
N-butyraldehyde	-0.48	e
2,4-Dipropyl-5-ethyl-1,3-dioxane	3.89	c
2-Ethylhexanol	2.73	c

e = experimental
c = calculated

Reliability : (2) valid with restrictions
Estimates using an acceptable method are assigned a reliability score of 2.

Flag : Critical study for SIDS endpoint

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2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in : Water
Value : at °C
pH value :
concentration : at °C
Temperature effects :
Examine different pol. :
pKa : at 25 °C
Description :
Stable :

Method :

Water solubility estimates and experimental values for the major components of EP-202 were obtained through the WSKOW program (v1.40) by entering the structure of the component into the program using the SMILES code. These codes are listed in the results section. Where there was an experimental value found in the database associated with the program, that value was accepted. Where an experimental value was not found the program estimate was accepted.

The following formula was used by the program to estimate the water solubility:

Log S (mol/L) = 0.796 - 0.854 log Kow - 0.00728 MW + Correction

The only Correction Value that was applied was for the two non-diol aliphatic alcohols.

Alcohol, aliphatic 0.510

Result :

The following results were obtained for water solubility:

COMPONENT	**SMILES****	Water Sol (mg/L)
2-Ethylhexenal	CCCC=C(CC)C=O	586 e
2-Ethylhexanal	CCCCC(CC)C=O	108 c
n-Butanol	CCCCO	6320 e
2-Ethyl-1,3-hexanediol	CCCC(O)C(CC)CO	4200 e
2-Ethylhexyl-1,3-dibutyrate	CCCC(OC(=O)CCC)C(CC)COC(=O)CCC	0.56 c
n-Butyl-n-butyrate	CCCC(=O)OCCCC	309 c
n-Butyraldehyde	CCCC=O	238 e
2,4-Dipropyl-5-ethyl-1,3-dioxane	C(CCC)1C(CC)COC(CCC)O1	20.7 c
2-Ethylhexanol	CCCCC(CC)CO	880 e

e = experimental
c = calculated

Test substance :

Components of EP-202

Conclusion :

Water solubility varies for components of EP-202 from less than 1 mg/L to 6800 mg/L.

Reliability : (2) valid with restrictions

Estimates using an acceptable method are assigned a reliability score of 2.

Flag : Critical study for SIDS endpoint

02.01.2004 (4)

3.1.1 PHOTODEGRADATION

Type : air
Light source :
Light spectrum : nm
Relative intensity : based on intensity of sunlight

Test substance :
Components of EP-202

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3.1.2 STABILITY IN WATER

Type : abiotic
t1/2 pH4 : at °C
t1/2 pH7 : at °C
t1/2 pH9 : at °C

Method : Water stability is estimated using chemical principles and HYDROWIN modeling.

Most of the components do not contain a water-reactive or hydrolysable group. The following are considered water stable* for this reason:
Aliphatic alcohols
Aliphatic ethers

The materials that are potentially hydrolysable are;
Aliphatic esters

These were entered into EPIWIN (HYDROWIN v1.67) to estimate hydrolysis rates using the following SMILES notations

Ref: J.C. Harris. Rate of Hydrolysis' in Handbook of Chemical Property Estimation Methods, WJ Lyman ed. ACS publication 1990.

Result : The following results were obtained for water stability:

```
HYDROWIN Program (v1.67) Results:
================================
SMILES : CCCC(OC(=O)CCC)C(CC)COC(=O)CCC
CHEM   : 2-Ethylhexyl-1,3-dibutyrate
MOL FOR: C16 H30 O4
MOL WT : 286.42
----------------- HYDROWIN v1.67 Results ---------------------------

NOTE: Fragment(s) on this compound are NOT available from the fragment
library. Substitute(s) have been used!!!  Substitute R1, R2, R3, or R4
fragments are marked with double astericks "**".

ESTER:  R1-C(=O)-O-R2                  R1: n-Propyl-
                                    ** R2: -CH(Me)(t-Bu)
 Kb hydrolysis at atom #  6:  1.455E-003  L/mol-sec


ESTER:  R1-C(=O)-O-R2                  R1: n-Propyl-
                                    ** R2: iso-Butyl-

 Kb hydrolysis at atom # 16:  3.416E-002  L/mol-sec

 Total Kb for pH > 8 at 25 deg C :  3.561E-002  L/mol-sec
 Kb Half-Life at pH 8:     225.252 days
 Kb Half-Life at pH 7:       6.167  years
```

```
SMILES : CCCC(=O)OCCCC
CHEM   : N-butyl-n-butyrate
MOL FOR: C8 H16 O2
MOL WT : 144.22
------- HYDROWIN v1.67 Results --------------------------

ESTER:  R1-C(=O)-O-R2                  R1: n-Propyl-
                                       R2: n-Butyl-
 Kb hydrolysis at atom #  4:  5.317E-002  L/mol-sec

 Total Kb for pH > 8 at 25 deg C :  5.317E-002  L/mol-sec
 Kb Half-Life at pH 8:     150.863 days
 Kb Half-Life at pH 7:       4.130  years
```

Test substance :

Components of EP-202

Conclusion :

Most components do not have a hydrolysable group and are considered stable, the two esters will be slowly hydrolyzed with estimated half-lives of greater than 1 year at pH 7.

Estimated Kb and half-live values are:

COMPONENT	Kb L/mol-s	half-life (yr) pH 7	pH 8
2-Ethylhexenal	0	>> 1	> 1
2-Ethylhexanal	0	>> 1	> 1
n-Butanol	0	>> 1	> 1
2-Ethyl-1,3-hexanediol	0	>> 1	> 1
2-Ethylhexyl-1,3-dibutyrate	0.0015	6.2	0.62
n-Butyl-n-butyrate	0.053	4.1	0.41
n-Butyraldehyde	0	>> 1	> 1
2,4-Dipropyl-5-ethyl-1,3-dioxane	0	>> 1	> 1
2-Ethylhexanol	0	>> 1	> 1

Reliability : (2) valid with restrictions

Estimates using an acceptable method are assigned a reliability score of 2.

Flag : Critical study for SIDS endpoint

02.01.2004 (5) (6)

3.3.2 DISTRIBUTION

Media : other: air, water, soil and sediment
Method : Calculation according Mackay, Level III
Year :

Method :

Theoretical Distribution (Fugacity) of EP-202 in the environment was estimated using the MacKay EQC level III model with standard defaults in EPIWIN v 3.05 using equal releases to water, soil and air (EPIWN default) as the means of entry into the environment. The approach used was to take the nine materials represented in the in the preparation at greater than 1% and individually determine their fugacity assuming that one component will not greatly affect the distribution of the other. As the measured vapor pressure of EP-202 is a function of the partial pressures of each component, it is more appropriate to use the EPIWIN predicted vapor pressure for each component in the calculation. Likewise, individual predicted values for log Kow, Koc, and half-lives were utilized. The biodegradation half-lives that were utilized were EPIWIN generated but were evaluated for consistency with the known biodegradability of the preparation and found to be representative.

Result :

```
Level III Fugacity Model (Full-Output):
=======================================
  Chem Name   : 2-Ethylhexenal
  Molecular Wt: 126.2
  Henry's LC  : 0.000488 atm-m3/mole (Henrywin program)
  Vapor Press : 0.463 mm Hg  (Mpbpwin program)
  Log Kow     : 2.62  (Kowwin program)
  Soil Koc    : 171  (calc by model)

         Concentration   Half-Life    Emissions
           (percent)        (hr)       (kg/hr)
  Air       1.39            4.21         1000
  Water     34.7            360          1000
  Soil      63.7            360          1000
  Sediment  0.216           1.44e+003    0

            Fugacity    Reaction    Advection   Reaction    Advection
             (atm)      (kg/hr)      (kg/hr)    (percent)   (percent)
  Air       1.73e-011    1.47e+003   89.2         49          2.97
  Water     4.31e-009    429         223          14.3        7.44
  Soil      1.99e-008    788         0            26.3        0
  Sediment  2.64e-009    0.669       0.0278       0.0223      0.000927

  Persistence Time: 214 hr
  Reaction Time:    239 hr
  Advection Time:   2.06e+003 hr
  Percent Reacted:  89.6
  Percent Advected: 10.4

  Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):
     Air:      4.207
     Water:    360
     Soil:     360
     Sediment: 1440
       Biowin estimate: 3.241  (weeks       )

  Advection Times (hr):
     Air:      100
     Water:    1000
     Sediment: 5e+004



Level III Fugacity Model (Full-Output):
=======================================
  Chem Name   : 2-Ethylhexanal
  Molecular Wt: 128.22
  Henry's LC  : 0.000759 atm-m3/mole (Henry database)
  Vapor Press : 2.18 mm Hg  (Mpbpwin program)
  Log Kow     : 2.71  (Kowwin program)
  Soil Koc    : 210  (calc by model)

         Concentration   Half-Life    Emissions
           (percent)        (hr)       (kg/hr)
  Air       2.58            7.56         1000
  Water     34.1            360          1000
  Soil      63              360          1000
  Sediment  0.241           1.44e+003    0

            Fugacity    Reaction    Advection   Reaction    Advection
             (atm)      (kg/hr)      (kg/hr)    (percent)   (percent)
  Air       3.05e-011    1.47e+003   160          48.9        5.33
  Water     6.26e-009    408         212          13.6        7.06
  Soil      2.4e-008     752         0            25.1        0
  Sediment  3.66e-009    0.719       0.0299       0.024       0.000996

  Persistence Time: 207 hr
  Reaction Time:    236 hr
  Advection Time:   1.67e+003 hr
  Percent Reacted:  87.6
  Percent Advected: 12.4

  Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):
     Air:      7.555
     Water:    360
     Soil:     360
     Sediment: 1440
       Biowin estimate: 3.236  (weeks       )
```

```
   Advection Times (hr):
      Air:      100
      Water:    1000
      Sediment: 5e+004


Level III Fugacity Model (Full-Output):
=======================================
  Chem Name   : n-Butanol
  Molecular Wt: 74.12
  Henry's LC  : 8.81e-006 atm-m3/mole (Henry database)
  Vapor Press : 7.78 mm Hg  (Mpbpwin program)
  Log Kow     : 0.88  (Kowwin program)
  Soil Koc    : 3.11  (calc by model)

         Concentration   Half-Life    Emissions
           (percent)        (hr)       (kg/hr)
   Air       5.91           30           1000
   Water     49.5           208          1000
   Soil      44.5           208          1000
   Sediment  0.0782         832          0

             Fugacity    Reaction    Advection   Reaction    Advection
              (atm)      (kg/hr)      (kg/hr)    (percent)   (percent)
   Air       1.05e-010    735         317         24.5        10.6
   Water     1.58e-010    886         266         29.5        8.87
   Soil      4.21e-009    796         0           26.5        0
   Sediment  1.16e-010    0.35        0.0084      0.0117      0.00028

   Persistence Time: 179 hr
   Reaction Time:    222 hr
   Advection Time:   920 hr
   Percent Reacted:  80.5
   Percent Advected: 19.5

   Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):
      Air:      29.95
      Water:    208.1
      Soil:     208.1
      Sediment: 832.3
        Biowin estimate: 3.494  (days-weeks  )

   Advection Times (hr):
      Air:      100
      Water:    1000
      Sediment: 5e+004




Level III Fugacity Model (Full-Output):
=======================================
  Chem Name   : 2-Ethyl-1,3-hexanediol
  Molecular Wt: 146.23
  Henry's LC  : 1.37e-008 atm-m3/mole (Henry database)
  Vapor Press : 0.003 mm Hg  (Mpbpwin program)
  Log Kow     : 1.6  (Kowwin program)
  Soil Koc    : 16.3  (calc by model)

         Concentration   Half-Life    Emissions
           (percent)        (hr)       (kg/hr)
   Air       0.34           11.5         1000
   Water     38.6           360          1000
   Soil      61             360          1000
   Sediment  0.0859         1.44e+003    0

             Fugacity    Reaction    Advection   Reaction    Advection
              (atm)      (kg/hr)      (kg/hr)    (percent)   (percent)
   Air       6.7e-012     241         40.1        8.02        1.34
   Water     2.13e-013    877         456         29.2        15.2
   Soil      5.42e-012    1.39e+003   0           46.2        0
   Sediment  1.71e-013    0.488       0.0203      0.0163      0.000676

   Persistence Time: 394 hr
   Reaction Time:    471 hr
   Advection Time:   2.38e+003 hr
   Percent Reacted:  83.5
   Percent Advected: 16.5
```

```
Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):
      Air:      11.55
      Water:    360
      Soil:     360
      Sediment: 1440
        Biowin estimate: 3.196  (weeks       )

   Advection Times (hr):
      Air:      100
      Water:    1000
      Sediment: 5e+004
```

```
Level III Fugacity Model (Full-Output):
=======================================
  Chem Name   : 2-Ethylhexyl-1,3-dibutyrate
  Molecular Wt: 286.42
  Henry's LC  : 3.7e-006 atm-m3/mole (Henrywin program)
  Vapor Press : 0.00147 mm Hg  (Mpbpwin program)
  Log Kow     : 5.17  (Kowwin program)
  Soil Koc    : 6.06e+004  (calc by model)

          Concentration   Half-Life    Emissions
            (percent)        (hr)       (kg/hr)
   Air       1.59            14.6         1000
   Water     27.7            360          1000
   Soil      48.5            360          1000
   Sediment  22.2            1.44e+003    0

             Fugacity    Reaction    Advection   Reaction    Advection
              (atm)      (kg/hr)      (kg/hr)    (percent)   (percent)
   Air       1.47e-011    816         172         27.2        5.75
   Water     1.77e-011    578         301         19.3        10
   Soil      2.59e-013    1.01e+003   0           33.7        0
   Sediment  5.33e-012    116         4.81        3.86        0.16

   Persistence Time: 361 hr
   Reaction Time:    430 hr
   Advection Time:   2.27e+003 hr
   Percent Reacted:  84.1
   Percent Advected: 15.9

   Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):
      Air:      14.64
      Water:    360
      Soil:     360
      Sediment: 1440
        Biowin estimate: 2.847  (weeks       )

   Advection Times (hr):
      Air:      100
      Water:    1000
      Sediment: 5e+004
```

```
Level III Fugacity Model (Full-Output):
=======================================
  Chem Name   : N-butyl-n-butyrate
  Molecular Wt: 144.22
  Henry's LC  : 0.000687 atm-m3/mole (Henry database)
  Vapor Press : 1.76 mm Hg  (Mpbpwin program)
  Log Kow     : 2.83  (Kowwin program)
  Soil Koc    : 277  (calc by model)

          Concentration   Half-Life    Emissions
            (percent)        (hr)       (kg/hr)
   Air       7.8             24.2         1000
   Water     35.2            208          1000
   Soil      56.8            208          1000
   Sediment  0.208           832          0

             Fugacity    Reaction    Advection   Reaction    Advection
              (atm)      (kg/hr)      (kg/hr)    (percent)   (percent)
   Air       6.17e-011    1.04e+003   364         34.7        12.1
   Water     3.91e-009    547         164         18.2        5.47
   Soil      1.01e-008    883         0           29.4        0
   Sediment  1.51e-009    0.808       0.0194      0.0269      0.000647
```

```
   Persistence Time: 156 hr
   Reaction Time:    189 hr
   Advection Time:   883 hr
   Percent Reacted:  82.4
   Percent Advected: 17.6

   Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):
      Air:      24.22
      Water:    208.1
      Soil:     208.1
      Sediment: 832.3
        Biowin estimate: 3.319  (days-weeks  )

   Advection Times (hr):
      Air:      100
      Water:    1000
      Sediment: 5e+004


Level III Fugacity Model (Full-Output):
=======================================
  Chem Name   : N-butyraldehyde
  Molecular Wt: 72.11
  Henry's LC  : 0.000115 atm-m3/mole (Henry database)
  Vapor Press : 108 mm Hg  (Mpbpwin program)
  Log Kow     : 0.88  (Kowwin program)
  Soil Koc    : 3.11  (calc by model)

          Concentration   Half-Life    Emissions
            (percent)        (hr)       (kg/hr)
   Air       3.68            10.9         1000
   Water     53.5            360          1000
   Soil      42.7            360          1000
   Sediment  0.095           1.44e+003    0

             Fugacity    Reaction    Advection   Reaction    Advection
              (atm)      (kg/hr)      (kg/hr)    (percent)   (percent)
   Air       7.34e-011    1.38e+003   217         45.8        7.23
   Water     2.51e-009    607         315         20.2        10.5
   Soil      5.95e-008    485         0           16.2        0
   Sediment  2.08e-009    0.27        0.0112      0.00898     0.000373

   Persistence Time: 197 hr
   Reaction Time:    239 hr
   Advection Time:   1.11e+003 hr
   Percent Reacted:  82.3
   Percent Advected: 17.7

   Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):
      Air:      10.92
      Water:    360
      Soil:     360
      Sediment: 1440
        Biowin estimate: 3.062  (weeks       )

   Advection Times (hr):
      Air:      100
      Water:    1000
      Sediment: 5e+004
```

```
Level III Fugacity Model (Full-Output):
=======================================
  Chem Name   : 2,4-Dipropyl-5-ethyl-1,3-dioxane
  Molecular Wt: 200.32
  Henry's LC  : 0.000286 atm-m3/mole (Henrywin program)
  Vapor Press : 0.0433 mm Hg  (Mpbpwin program)
  Log Kow     : 3.89  (Kowwin program)
  Soil Koc    : 3.18e+003  (calc by model)

          Concentration   Half-Life    Emissions
            (percent)        (hr)       (kg/hr)
   Air       0.604           5.06         1000
   Water     19.7            900          1000
   Soil      77.6            900          1000
   Sediment  2.13            3.6e+003     0

             Fugacity    Reaction    Advection   Reaction    Advection
              (atm)      (kg/hr)      (kg/hr)    (percent)   (percent)
   Air       1.2e-011     1.35e+003   98.6         45          3.29
   Water     2.28e-009    247         321          8.24        10.7
   Soil      1.31e-009    976         0            32.5        0
   Sediment  1.61e-009    6.71        0.697        0.224       0.0232

   Persistence Time: 544 hr
   Reaction Time:    633 hr
   Advection Time:   3.88e+003 hr
   Percent Reacted:  86
   Percent Advected: 14

   Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):
      Air:      5.064
      Water:    900
      Soil:     900
      Sediment: 3600
        Biowin estimate: 2.739  (weeks-months)

   Advection Times (hr):
      Air:      100
      Water:    1000
      Sediment: 5e+004


Level III Fugacity Model (Full-Output):
=======================================
  Chem Name   : 2-Ethylhexanol
  Molecular Wt: 130.23
  Henry's LC  : 2.65e-005 atm-m3/mole (Henry database)
  Vapor Press : 0.185 mm Hg  (Mpbpwin program)
  Log Kow     : 2.73  (Kowwin program)
  Soil Koc    : 220  (calc by model)

          Concentration   Half-Life    Emissions
            (percent)        (hr)       (kg/hr)
   Air       4.24            19.4         1000
   Water     41.2            208          1000
   Soil      54.3            208          1000
   Sediment  0.216           832          0

             Fugacity    Reaction    Advection   Reaction    Advection
              (atm)      (kg/hr)      (kg/hr)    (percent)   (percent)
   Air       4.31e-011    820         230          27.3        7.66
   Water     2.27e-010    745         224          24.8        7.45
   Soil      5.96e-010    981         0            32.7        0
   Sediment  9.5e-011     0.977       0.0235       0.0326      0.000782

   Persistence Time: 181 hr
   Reaction Time:    213 hr
   Advection Time:   1.2e+003 hr
   Percent Reacted:  84.9
   Percent Advected: 15.1

   Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):
      Air:      19.4
      Water:    208.1
      Soil:     208.1
      Sediment: 832.3
        Biowin estimate: 3.370  (days-weeks  )

   Advection Times (hr):
      Air:      100
      Water:    1000
      Sediment: 5e+004
```

Test substance :

Components of EP-202

Conclusion :

The components of EP-202 distribute primarily to water and soil with little in the air or sediment except for the two esters, with n-butyl butyrate being more volatile and 2-ethylhexyl-1,3-dibutyrate distributing in sediment to a significant extent. Summary results are shown below.

	Air	Water	Soil	Sediment
2-Ethylhexenal	1.39	34.7	63.7	0.216
2-Ethylhexanal	2.58	34.1	63.0	0.241
n-Butanol	5.91	49.5	44.5	0.0782
2-Ethyl-1,3-hexanediol	0.34	38.6	61.0	0.0859
2-Ethylhexyl-1,3-dibutyrate	1.59	27.7	48.5	22.2
2,4-Dipropyl-5-ethyl-1,3-dioxane	0.604	19.7	77.6	2.13
n-Butyl-n-butyrate	7.8	35.2	56.8	0.208
n-Butyraldehyde	3.68	53.5	42.7	0.095
2-Ethylhexanol	4.24	41.2	54.3	0.216

Reliability : (2) valid with restrictions

Estimates using an acceptable method are assigned a reliability score of 2.

Flag : Critical study for SIDS endpoint

03.01.2004 (7)

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	semistatic
Species	:	Cyprinus carpio (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC0	:	= 3 measured/nominal
LC50	:	= 6 measured/nominal
LC100	:	= 12 measured/nominal
Limit test	:	no
Analytical monitoring	:	yes
Method	:	Directive 84/449/EEC, C.1 "Acute toxicity for fish"
Year	:	1992
GLP	:	yes
Test substance	:	other TS
Remark	:	Multiple aquatic studies are available for this material at all trophic levels. This study was selected as it had the lowest EC50 for fish and was conducted under GLPs.
Source	:	IUCLID 2000 Document
Test substance	:	2-Ethylhexenal CASNO 645-62-5
Reliability	:	(1) valid without restriction Guideline study under GLPs from IUCLID 2000. Supporting studies increase reliability.
Flag	:	Critical study for SIDS endpoint

03.01.2004 (8)

Type	:	static
Species	:	Salmo gairdneri (Fish, estuary, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
LC0	:	= 6.3 measured/nominal
LC50	:	= 8 measured/nominal
LC100	:	= 10 measured/nominal
Method	:	OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year	:	1979
GLP	:	
Test substance	:	other TS
Remark	:	Two other acute fish studies are reported for this material in IUCLID 2000 that give similar results in other species (Lepomis gibbosus, LC50 11 mg/l; Leuciscus idus. LC50 10-32 mg/L). This study selected because it has the lowest LC50.
Test substance	:	2-Ethylhexanal CASNO 123-05-7 purity 99%
Reliability	:	(2) valid with restrictions Guideline study from IUCLID 2000 without many details. Supporting studies available on same material increases reliability.
Flag	:	Critical study for SIDS endpoint

03.01.2004 (9)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:	other: no data
Species	:	Daphnia magna (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
EC0	:	= 12.5 measured/nominal
EC50	:	= 20 measured/nominal
EC100	:	= 50 measured/nominal
Limit Test	:	no
Analytical monitoring	:	no data
Method	:	Directive 84/449/EEC, C.2 "Acute toxicity for Daphnia"
Year	:	1984
GLP	:	no data
Test substance	:	other TS
Remark	:	Multiple aquatic studies are available for this material at all trophic levels. This study was selected as it had the lowest EC50 for daphnids.
Test substance	:	2-Ethylhexenal CASNO 645-62-5
Reliability	:	(2) valid with restrictions Guideline study from IUCLID 2000. Supporting studies increase reliability.
Flag	:	Critical study for SIDS endpoint

03.01.2004 (10)

Type	:	other: no data
Species	:	Daphnia magna (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
EC0	:	= 6.25 - 11.5 measured/nominal
EC50	:	= measured/nominal
EC100	:	= 25 measured/nominal
Method	:	Directive 84/449/EEC, C.2 "Acute toxicity for Daphnia"
Year	:	
GLP	:	no data
Test substance	:	other TS
Remark	:	Only daphnia study available for chemical.
Test substance	:	2-Ethylhexanal CASNO 123-05-7
Reliability	:	(2) valid with restrictions Guideline study from IUCLID 2000 without many details included. Supporting studies available for similar materials increases reliability.
Flag	:	Critical study for SIDS endpoint

03.01.2004 (11)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	Scenedesmus subspicatus (Algae)
Endpoint	:	growth rate
Exposure period	:	72 hour(s)
Unit	:	mg/l
EC50	:	= 19.3 measured/nominal
EC90	:	= 54 measured/nominal
EC20	:	= 12.8 measured/nominal
Method	:	other: Algentest in Anlehnung an UBA
Year	:	
GLP	:	
Test substance	:	other TS
Remark	:	Multiple aquatic studies are available for this material at all trophic levels. This study was selected as it had the lowest EC50 for green algae.
Test substance	:	2-Ethylhexenal CASNO 645-62-5
Reliability	:	(2) valid with restrictions Guideline study from IUCLID 2000. Supporting studies increase reliability.
Flag	:	Critical study for SIDS endpoint

03.01.2004 (12)

Species	:	Scenedesmus subspicatus (Algae)
Endpoint	:	growth rate
Exposure period	:	96 hour(s)
Unit	:	mg/l
EC50	:	= 52 measured/nominal
EC20	:	= 36 measured/nominal
EC90	:	= 111 measured/nominal
Method	:	other: Scenedesmus-Zellvermehrungs-Hemmtest, DIN 38412 Teil 9, Bestimmung der Hemmwirkung von Wasserinhaltsstoffen auf Gruenalgen
Year	:	
GLP	:	
Test substance	:	
Remark	:	Only green algae study available for chemical.
Test substance	:	2-Ethylhexanal CASNO 123-05-7
Reliability	:	(2) valid with restrictions Guideline study from IUCLID 2000 without many details. Supporting studies available for similar materials increases reliability.
Flag	:	Critical study for SIDS endpoint

03.01.2004 (13)

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Value	:	> 5000 mg/kg bw
Species	:	rat
Strain	:	Wistar
Sex	:	male/female
Number of animals	:	20
Vehicle	:	other: olive oil
Doses	:	2000 or 5000 mg/kg bw
Method	:	other: Directive 83/467/EWG
Year	:	1983
GLP	:	yes
Test substance	:	

Method :

Groups of five overnight-fasted Wistar rats were dosed at 5000 or 2000 mg/kg with test material in olive oil. After administration animals were observed for a period of 14 days, sacrificed and examined for signs of adverse effects. Animal weights (as group mean) were recorded at the beginning of the study and on days 3, 5, 7 and 13.

Remark :

Oxooel 740 is the BASF designation for the heavy fraction from the distillation of the butanols. In Germany, the hydroformylation chemistry is practiced with slight modification and the heavy ends from the distillation of the aldehydes is not blended with the heavy ends from distillation of the alcohols. As discussed in the HPV testing plan, the chemical reactions producing the heavy fraction are essentially identical and the compositions of the US product EP-202MP and the German equilivent product Oxooel 740 are very similar, both are variable and both share the same CAS registry number. The only difference is that the EP-204MP has a slightly higher quantity of C4 compounds.

Result : One 5000-mg/kg male died on day 1. No other animal died on test.

Body weight gain was normal in treated females but appeared to be slightly retarded in 5000-mg/kg males.

Clinical sings of intoxication were not observed at 2000 mg/kg. At 5000 mg/kg males showed more severe signs consisting of dyspnea, apathy, atonia, staggering, piloerection, and similar sings estednedg to 3 days after treatment. High dose females showed similar clinical signs but to a lesser degree and they only persisted for one day.

Test substance :

Oxooel 740 ROH (German production material corresponding with US EP-202)

Conclusion :

The LD50 for this material in Wistar rats of each sex is > 5000 mg/kg. No target organs were identified. Males may be the more sensitive sex.

Reliability : (1) valid without restriction

Guideline study under GLPS

Flag : Critical study for SIDS endpoint

07.06.2004 (14)

5.1.2 ACUTE INHALATION TOXICITY

5.1.3 ACUTE DERMAL TOXICITY

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.4 REPEATED DOSE TOXICITY

Type	:	Sub-chronic
Species	:	rat
Sex	:	male/female
Strain	:	Fischer 344
Route of admin.	:	gavage
Exposure period	:	13 weeks
Frequency of treatm.	:	5 days/week
Post exposure period	:	none
Doses	:	0, 25, 125, 250 or 500 mg/kg-bw
Control group	:	yes, concurrent vehicle
NOAEL	:	= 125 mg/kg bw
LOAEL	:	= 250 mg/kg bw
Method	:	
Year	:	
GLP	:	no data
Test substance	:	other TS

Method :

Animals. F344 rats, 36- to 37-days-old at delivery, were kept singly in stainless steel wire cages. Mean body weight ranges at dosing were (male) 105-114 g and (female) 86-97 g. Animals were acclimated 6 days on a 12-hr photoperiod at 20-24°C and 30-70% relative humidity; food and water were ad lib.

In the 13-week study groups of 10 animals of each sex rats received daily oral gavage doses of 0, 25, 125, 250 or 500 mg/kg on 5 consecutive days per week. Doses were prepared daily by dispersing TS in an aqueous solution of Cremophor EL (5 mg/100 ml). Dosing volume was 10 ml/kg, based on weekly body weights. Controls received 5.0 ml/kg vehicle. Concentrations and homogeneity were checked by gas chromatographic analysis of samples from each dose level at study start and periodically during the 13-week study. Animals were fasted for about 16 hr after the last dose and terminated by decapitation under CO_2 anesthesia.

In-life observations. Animals were inspected twice daily for morbidity and mortality but only once daily on nontreatment days. Clinical observations were made daily. Body weights were determined on day 01 and weekly thereafter. Animals were palpated on weighing. Average daily food consumption was determined weekly. Blood was collected by retroorbital bleeding from fasted animals on the morning of Days 29 and 84. Standard serum enzyme activities and biochemistry measurements were recorded. Hematology parameters were leucocytes, erythrocytes, hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin,

mean corpuscular hemoglobin concentration, platelets, differential leucocytes, and reticulocytes.

Observations at necropsy. Moribund animals were euthanized and dead and euthanized animals were immediately necropsied for gross pathology. At scheduled terminations body and organ weights were measured. At study termination adrenals, brains, kidneys, livers, stomachs, testes, and ovaries from all animals were weighed, and with other organs and tissues listed in U.S. EPA Health Effects Guidelines (1987b) fixed in 4% formalin. All tissues from high dose and control animals were stained with hematoxylin-eosin and examined microscopically. Lungs, livers, spleens, kidneys, stomachs, sternums, femurs, and femur bone marrows were examined microscopically at intermediate dose levels. Skin, eyes, female mammary glands, thigh musculatures, and extraorbital lacrymatory glands were not examined in the absence of signs of toxicity. Livers were also stained with oil red for reticulolipid content and examined microscopically.

Ancillary studies were used only to determine hepatic peroxisome proliferation. Livers were removed at termination and weighed, and cyanide-insensitive pCoA activities and protein concentrations were determined.

Statistical treatment of data. Means and standard deviations were calculated for body weights, food and water consumption, clinical pathology results, and organ weights. Values for test groups were compared with controls in the main study by ANOVA followed by Dunnett's test.

Result :

No rat died on test. There was deacreased weight gain in male and female rats at 500 mg/kg, starting at Week 4 in males and Week 11 in females, amounting to weight losses of 7% in males and 6% in females by Week 13. There were no differences from controls at any treatment level in food consumption.

Clinical pathology. Differences from control values were seen mostly at 84 days. Females at 250 and 500 mg/kg had 30 and 36% decreases in serum ALT activities, respectively. Females at 500 mg/kg had a 16% decrease in serum cholesterol concentration and males at 500 mg/kg had 13% decreases in total protein and albumin
concentrations. There was a 25% increase in reticulocyte numbers in male and female rats at 500 mg/kg.

Necropsy findings: Relative organ weights. Significant differences from controls in rats were moderate and limited to the brain, kidneys, liver, stomach, and testes at 250 and 500 mg/kg (Table 3). Male rat relative brain weights increased by 6% at 500 mg/kg, male kidney weights by 8% at 250 and 16% at 500 mg/kg, male liver weights by 8% at 250 and 29% at 500 mg/kg, male stomach weights by 11%
at 500 mg/kg, and testis weights by 5.5% at 500 mg/kg. Female's kidney weights increased by 5% at 250 and 6% at 500 mg/kg, female liver weights by 8% at 250 and 15% at 500 mg/kg, and female stomach weights by 6% at 250 and 16% at 500 mg/kg.

Necropsy findings: Gross observations. Gross lesions differing from controls 500 mg/kg only. 2/10 males and 4/10 females exhibited single or multiple slightly elevated foci in the forestomach. There were no other gross findings.

Necropsy findings: Microscopic findings. Dose-related findings were limited to the forestomach and liver at 500 mg/kg. There was a generalized acannothosis of the forestomach mucosa in 1/10 males with ballooning degeneration of the epithelial wall and acanthosis of the forestomach mucosa in 2/10 males and 5/10 females.
There was a moderate decrease in hepatic peripheral lobular fatty infiltration in 4/10 males and 2/10 females and adrenal b-cell hyperplasia in 3/10 females.

Peroxisome proliferation. Hepatic peroxisome proliferation was determined in ancillary 13-week studies by measuring activity of hepatic cyanide-insensitive palmitoyl Coenzyme A in livers at termination. Increases in pCoA activity were 6.5-fold in male rats and 3.4-fold in females at 500 mg/kg, with decreases in body weight gain similar to those in the main study.

Relative Organ Weights at Termination (grams (SD))
Weights at other dose levels (25 and 125 mg/kg) did not differ from controls.

Males	0	250	500
Brain	0.68 (0.03)	0.70 (0.02)	0.72 (0.02)**
Kidneys	0.69 (0.02)	0.75 (0.02)**	0.81 (0.04)**
Liver	2.77 (0.11)	2.98 (0.08)**	3.57 (0.22)**
Stomach	0.57 (0.03)	0.58 (0.03)	0.63 (0.02)**
Testes	1.11 (0.05)	1.16 (0.07)	1.17 (0.06)*

Females	0	250	500
Brain	1.07 (0.03)	1.1 (0.06)	1.1 (0.04)
Kidneys	0.77 (0.02)	0.81 (0.03)*	0.82 (0.03)**
Liver	2.67 (0.11)	2.88 (0.08)**	3.07 (0.07)**
Stomach	0.71 (0.03)	0.75 (0.03)*	0.82 (0.04)**
Ovaries	0.041(0.003)	0.037(0.005)*	0.039(0.004)

*p 0.05
** p 0.01

Test substance :

2-Ethylhexanol CASNO 104-76-7 (component and surrogate)
Purity 99.8% purity by gas chromatography.

Conclusion :

The 500-mg/kg dose was associated with significant peroxisome proliferation and systemic toxicity as evidenced by small but statistically significant ($p < 0.01$) reduction in weight gain in rats of each sex. Target organs were the liver and forestomach. The possible testes effects were of special interest and there was a slight increase in relative testis weight at 500 mg/kg but this was not correlated with any morphological changes. The reduced relative ovarian weight at 250 mg/kg did not occur at 500 mg/kg and is considered incidental. It is concluded that 125 mg/kg was a NOEL based on organ weight changes at 250 mg/kg.

Reliability : (2) valid with restrictions

Published studies are assigned a 2

Flag : Critical study for SIDS endpoint

05.01.2004 (15)

5.5 GENETIC TOXICITY 'IN VITRO'

Type	:	Bacterial reverse mutation assay
System of testing	:	Salmonella
Test concentration	:	Varies
Cycotoxic concentr.	:	See Results
Metabolic activation	:	with and without
Result	:	negative
Method	:	other: National Toxicology Program
Year	:	
GLP	:	no data
Test substance	:	other TS

Method :

As each stain of Salmonella typhimurium is genetically different, using several strains in a test increases the opportunity of detecting a mutagenic chemical. All strains of Salmonella typhimurium used for mutagenicity testing carry a defective (mutant) gene that prevents them from synthesizing the essential amino acid histidine. Mutations leading to the ability to sysntesize histidine are called "back" or "reverse" mutations and the process is referred to as "reversion."

Some test protocols utilize extracts of Aroclor rat or hamster liver enzymes (S9) to promote metabolic conversion of the test chemical. This is necessary since the Salmonella bacterium does not have the mamillian metabolic capabilities.

In the Salmonella assay, a test tube containing a suspension of one strain of Salmonella typhimurium plus S9 mix or plain buffer without S9, is incubated for 20 minutes at 37º C with the test chemical. Control cultures, with all the same ingredients except the test chemical, are also identically incubated. In addition, positive controls with a known potent mutagen, are prepared. After 20 minutes, agar is added to the cultures and the contents of the tubes are thoroughly mixed and poured onto the surface of petri dishes containing standard bacterial culture medium. The plates are incubated, and bacterial colonies that do not require an excess of supplemental histidine appear and grow. These colonies are comprised of Salmonella that have undergone reverse mutation to restore function of the histidine-manufacturing gene. The number of colonies is counted after 2 days.

Several doses (at least 5) of each test chemical and multiple strains of Salmonella typhimurium are used in each experiment. In addition, cultures are set up with and without added S9 liver enzymes at 10% concentration in these studies.

The pattern and the strength of the mutant response are taken into account in determining the mutagenicity of a chemical. All observed responses are verified in repeat tests. If no increase in mutant colonies is seen after testing several strains under several different culture conditions, the test chemical is considered to be nonmutagenic in the Salmonella test.

Reference
Mortelmans K, Zeiger E. The Ames Salmonella/microsome mutagenicity assay. Mutat Res. 2000 Nov 20;455(1-2):29-60.

Result :

Summary Information
Study Vehicle: DMSO
Protocol: Preincubation
Result: Negative

Strain: TA100

Dose	No Act (Neg)		No Act (Neg)		10% RLI (Neg)		10% RLI (Neg)		10% HLI (Neg)		10% HLI (Neg)	
ug/Pt.	Mean	sem	Mean	sem	Mean	sem	Mean	sem	Mean	sem	Mean	sem
VC	130	0.3	133	2.9	101	10.7	100	4	124	7.8	124	8.2
3.3	123	1.9	118	9.6	116	39.1	122	3.8	116	16.3	127	42.2
10	137	4.6	111	7.5	119	1	109	10.4	111	9.9	129	43.6
33	134	4.9	115	12.5	115	5.9	116	10.7	117	8.4	99	3.5
100	115	4.5	137	1.8	107	7.2	96	1.7	110	12.4	112	8.8
220			109s	4.9			114	14.5			126	5.4
333	21	0			158	0			180	0		
PC	1133	52	1284	34	800	36	1379	56	973	95.7	1459	98.6

Strain: TA1535

Dose	No Act (Neg)		No Act (Neg)		10% RLI (Neg)		10% RLI (Neg)		10% HLI (Neg)		10% HLI (Neg)	
ug/Pt.	Mn	sem	Mean	sem	Mean	sem	Mean	sem	Mean	sem	Mean	sem
VC	27	3	33	2.3	11	0.7	17	3.8	15	3.2	13	2.7
3.3	27	3.8	33	1	14	1.8	17	1	14	2.1	17	2.6
10	27	3	27	2.7	15	1.8	14	0.3	16	4.1	14	2.6
33	27	1.2	35	0.3	15	1.2	14	1.7	12	3.8	18	0.6
100	22	4.3	31	2.2	12	1.8	13	1.3	13	0.6	14	1
220			25s	2.6			14	0.6			14	2.9
333	T	0			8	0			5s	1.8		
PC	835	13	902	21	66	3.8	91	10.2	84	3.9	90	2.6

Strain: TA1537

Dose	No Act (Neg)		No Act (Neg)		No Act (Neg)		10% RLI (Neg)		10% RLI (Neg)		10% HLI (Neg)		10% HLI (Neg)	
ug/Pt.	Mean	sem	Mean	sem	Mea	sem	Mn	sem	Mn	sem	Mn	sem	Mean	sem
VC	6	0.7	6	0.3	5	0.7	6	1.2	6	0.9	6	1	9	2.6
3.3	8	1.2	4	0.6	6	1.5	5	0.3	7	2.1	5	1.2	9	1.7
10	11	1.9	5	1.2	8	1.9	7	2.5	8	1.5	6	1.5	8	2.2
33	11	2.3	6	0.9	5	0.6	7	1	4	0.7	6	1.2	7	1.5
100	13	2.3	5	1.5	7	2	5	0.7	8	1.8	6	1.2	9	0.9
220					6s	1.7			9	1.2			8	2.6
333	173	0	339	0			12s	2			188s	1		
PC	133	10.7	468	69	370	59	73	4.3	98	11.7	82	7.7	117	38.9

Strain: TA98

Dose	No Act (Neg)		No Act (Neg)		10% RLI (Neg)		10% RLI (Neg)		10% HLI (Neg)		10% HLI (Neg)	
ug/Pt.	Mean	sem	Mn	sem	Mean	sem	Mean	sem	Mean	sem	Mean	sem
VC	17	1.3	18	1.5	20	1.2	20	2.6	28	4.9	33	4.9
3.3	18	1.3	17	2.6	20	3.2	22	1.5	30	0.9	24	4.7
10	12	1.2	15	2.3	23	0.7	23	1.5	24	2	29	0.3
33	16	2	22	1.2	24	4.2	24	3.2	20	2	28	3.2
100	19	1.5	19	0.6	22	2.9	25	1.3	26	1.7	26	1.7
220			18s	1			27	2.1			29	2.6
333	210	0			305	0			9s	3.8		
PC	1049	31	1289	46	544	17	855	31	960	59	820	37.5

Abbreviations:
PC = positive control
VC = vehicle control
RLI = induced male Sprague Dawley rat liver S9
HLI = induced male Syrian hamster liver S9
s = Slight Toxicity; p = Precipitate; x = Slight Toxicity and Precipitate; T = Toxic; c = Contamination

Test substance :

2-Ethylhexanol CASNO 104-76-7 (component and surrogate)

Conclusion : Material was non-mutagenic in the presence or absence of standard liver metabolic activating systems

Reliability : (1) valid without restriction

NTP Guideline study with data for review.

Flag : Critical study for SIDS endpoint

04.01.2004 (16)

Type	:	Chromosomal aberration test
System of testing	:	Chinese hamster ovary cells (CHO-W-B1)
Test concentration	:	see results
Cycotoxic concentr.	:	see results
Metabolic activation	:	with and without
Result	:	negative
Method	:	other: NTP Protocol
Year	:	
GLP	:	
Test substance	:	other TS

Method :

An in vitro assay for chromosomal damage was conducted in cloned Chinese hamster ovary cells (CHO-W-B1) to identify chemicals capable of inducing chromosomal aberrations (CA). The procedure is described in detail by Galloway et al. (1985, 1987). This assay only detects structural chromosomal damage; it does not detect aneuploidy.

Test chemicals were supplied to the testing laboratory as coded aliquots. The substance was tested in cultured CHO cells for induction of SCE and CA, both in the presence and absence of Aroclor 1254-induced male Sprague Dawley rat liver S9 enzymes and cofactor mix. Cultures were handled under gold lights to prevent photolysis of bromodeoxyuridine-substituted DNA. Each test consisted of concurrent solvent and positive controls and of at least three concentrations of test substance; the high dose was limited by toxicity or solubility, or in the absence of either of these factors, the high dose was limited to 5 mg/mL . A single culture flask per concentration was used. Tests yielding equivocal or positive results generally were repeated.

Cells were harvested in their first mitotic division after the initiation of chemical exposure. Without S9, cells were incubated for 8-12 hours with the test chemical in McCoy's 5A medium supplemented with fetal calf serum, L-glutamine, and antibiotics, then Colcemid was added and incubation was continued for 2 hours. The incubation time and the dose levels selected were determined from the information on cell cycling and toxicity obtained from the prior SCE test; if cell cycle delay was anticipated, the incubation period was extended to permit accumulation of sufficient cells in first metaphase for statistical analysis. The cells were harvested by mitotic shake-off, fixed, and stained with Giemsa. For the CA test with S9, cells were treated with the test chemical and S9 for 2 hrs, after which the treatment medium was removed and the cells incubated for 10 hours in fresh medium, with Colcemid present for the final 2 hrs. Cells were harvested in the same way as for the treatment without S9.

Cells were selected for scoring on the basis of adequate morphology and completeness of karyotype (21 +/- 2 chromosomes). All slides were scored blind and those from a single test were read by the same person. One hundred or two hundred first-division metaphase cells were scored at each dose level. The classes of aberrations that were recorded included "simple" (breaks and terminal deletions), "complex" (rearrangements and translocations), and "other" (pulverized cells, despiralized chromosomes, and cells containing 10 or more aberrations).

Data are presented as the percentage of cells with aberrations. To arrive at a statistical call for a trial, analyses were conducted to assess the presence of a dose-response (trend test) and the significance of the individual dose points compared to the vehicle control (Galloway et al., 1987). For a single trial, a statistically significant ($P<0.05$) difference for one dose point and a significant trend ($P<0.015$) was considered weak evidence for a positive response; significant differences for two or more doses indicated the trial was positive. A strong trend ($P < 0.003$) with a single significant dose level was designated weak positive *, to indicate a high level of induced aberrations. A

strongly positive trend (P < 0.003), in the absence of a statistically-significant increase at any one dose point, led to an equivocal call. Ultimately, the trial calls were based on a consideration of the statistical analyses as well as the biological information available to the reviewers. Trials that gave a weak positive or positive result were repeated. The overall result for the CA assay was based on an evaluation of the responses in all trials within an activation condition.

Galloway SM, Armstrong MJ, Reuben C. et al. (1987) Chromosome aberrations and sister chromatid exchanges in Chinese hamster ovary cells: Evaluations of 108 chemicals. Environ. Mol. Mutagen. 10(Supplement 10): 1 - 175.

Galloway SM, Bloom AD, Resnick M et al. (1985) Development of a standard protocol for in vitro cytogenetic testing with Chinese hamster ovary cells: Comparison of results for 22 compounds in two laboratories. Environ. Mutagen. 7: 1-51.

Result :

Activation	Trial	Trial Call
No Activation	1	Negative
Induced Rat Liver S9	2	Negative

	Dose µg/mL	Cells	Total Abs. Abs #	Total Abs. Abs Per Cell	Total Abs. % With Abs.	Complex Abs. Abs #	Complex Abs. Abs Per Cell	Complex Abs. % With Abs.	Simple Abs. Abs #	Simple Abs. Abs Per Cell	Simple Abs. % With Abs.	Other Abs. % Ab With #	Other Abs. % Ab With Abs.
Neg	0	100	0	0	0	0	0	0	0	0	0	0	0
DMSO	0	200	1	0.005	0.5	0	0	0	1	0.01	0.5	0	0
TS	50	200	3	0.015	1	1	0.01	0.5	2	0.01	1	0	0
TS	108	200	1	0.005	0.5	1	0.01	0.5	0	0	0	0	0
TS	233	200	2	0.01	1	0	0	0	2	0.01	1	0	0
TS	500	0	0	0	0	0	0	0	0	0	0	0	0
Mito	0.1	200	40	0.2	16	21	0.11	9	19	0.1	9.5	0	0
	0.4	50	18	0.36	26	11	0.22	18	7	0.14	14	0	0
Trend:			0.366			-0.001			0.2				
Probability:			0.357			0.5			0.421				

	Dose µg/mL	Cells	Total Abs. Abs #	Total Abs. Abs Per Cell	Total Abs. % With Abs.	Complex Abs. Abs #	Complex Abs. Abs Per Cell	Complex Abs. % With Abs.	Simple Abs. Abs #	Simple Abs. Abs Per Cell	Simple Abs. % With Abs.	Other Abs. % Ab With #	Other Abs. % Ab With Abs.
Neg	0	100	0	0	0	0	0	0	0	0	0	0	0
DMSO	0	200	1	0.005	0.5	0	0	0	1	0.01	0.5	0	0
TS	50	200	0	0	0	0	0	0	0	0	0	0	0
TS	108	200	0	0	0	0	0	0	0	0	0	0	0
TS	233	200	5	0.025	1.5	1	0.01	0.5	4	0.02	1.5	0	0
TS	500	0	0	0	0	0	0	0	0	0	0	0	0
Cyclo	5	200	32	0.16	11.5	12	0.06	5	20	0.1	7.5	0	0
	15	50	11	0.22	20	6	0.12	10	5	0.1	10	0	0
Trend:			1.346			1.343			1.346				
Probability:			0.089			0.09			0.089				

Test substance :

2-Ethylhexanol CASNO 104-76-7 (component and surrogate)

Conclusion :

Material did not induce chromosome aberrations in presence or absence of a metabolic activation system

Reliability : (1) valid without restriction

NTP Guideline study with data for review.

Flag : Critical study for SIDS endpoint

04.01.2004 (16)

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species	:	mouse
Sex	:	female
Strain	:	CD-1
Route of admin.	:	oral feed
Exposure period	:	gd 1 to 17
Frequency of treatm.	:	cont
Duration of test	:	
Doses	:	90, 300 or 900 ppm
Control group	:	yes, concurrent vehicle
Method	:	
Year	:	
GLP	:	
Test substance	:	other TS

Method :

Groups of 28 pregnant Swiss (CD-1) mice were treated with 2-ethylhexanol (2EH) in feed at 0, 90, 300 or 900 ppm in feed (corresponding to 0, 0.13, 0.46, 1.49 mmol/kg-day)in a microencapsulated form to prevent reaction with feed and loss of bioavailability. Dosed feed was provided as lib from gestational day 0 to gestational day 17, at which time dams were sacrificed and the products of conception were evaluated. At sacrifice, the number of ovarian corpora lutea and uterine implantation sites, including resorptions, and dead or live fetuses, were recorded. Live and dead fetuses were weighed. Live fetuses were sexed and examined for external, visceral and skeletal malformations and variations using the standard protocols employed by the NTP for developmental toxicity evaluations in mice.

For comparative purposes, groups of pregnant mice were administered mono-2-ethylhexylphthalate (MEHP) at 0, 0.13, 0.26, 0.48, 0.97 mmol/kg-day from day 0 to gd 17 of pregnancy. Dams were sacrificed and developmental toxicity was evaluated using the same procedure as used for 2EH.

Remark :

The maximum administered dose of 2-ethylhexanol was approximately 190 mg/kg-day. This dose produced neither maternal toxicity nor developmental toxicity. Ideally, a robust test of the developmental toxicity of 2-ethylhexanol would have included a dose level that produced maternal toxicity. In light of the finding that MEHP produced developmental toxicity at dose levels only one-sixth the maximum dose of 2-ethylhexanol that was administered, it is concluded that 2-ethylhexanol has no developmental toxicity at doses up to 190 mg/kg-day.

Support for a lack of developmental toxicity of 2-ethylhexanol comes from the di-2-ethylhexyl adipate fertility and developmental toxicity study in which a dose of 1080 mg/kg-day to Wistar rats was associated with minimal fetotoxicity and maternal toxicity. [ICI. 1988b. ICI Central Toxicology Laboratory. Di-(2-ethylhexyl)adipate (DEHA): Fertility study in rats. Report CTL/P/2229 (unpublished study). As cited in IRIS, US EPA.]

There is also a dermal developmental toxicity in which groups of 25 pregnant female Fischer 344 rats were treated cutaneously with 2-ethylhexanol at dose levels of 0, 0.3, 1.0, or 3.0 ml/kg/day for 6 hours per day on gestation days 6 through 15. No treatment-related maternal deaths or early pregnancy loss were seen in the treatment groups, but maternal

weight gain was significantly reduced during gestation day 6 through 9 in the high-dose animals. Exfoliation and crusting were seen at treatment sites at all dose levels and erythema at dose levels 1.0 and 3.0 ml/kg-day. Low-dose groups, showed an increase in postimplantation loss, decreased litter size, and reduced fetal body weights but this was not observed in the high-dose group. There were no significant increases in incidence of malformations in the 2-ethylhexanol group relative to the sham treatment group. It is concluded that 2-ethylhexanol has no developmental toxicity activity by the dermal route in rats. [Developmental toxicity evaluation of 2-ethylhexanol administered cutaneously to Fischer 344 rats (final report) with attachments and cover letters dated 032189 and 050389, Bushy Run Research Center, EPA/OTS; Doc #86-890000216}

Result :

In the groups treated with 2-ethylhexanol no dams died, delivered early or were removed from study. The pregnancy rate was high (93-96%) and similar in all groups. In the control group, one litter was fully resorbed. All other pregnant animals had live litters at the gd-17 necropsy. The numbers of live litters evaluated were 27 at 90 and 300 ppm and 26 at 0 and 900 ppm levels. No maternal toxicity observed in this study as a result of 2-ethylhexanol administration. Maternal body weights, absolute weight gains, corrected weight gains, gravid uterine weight absolute liver weight and relative liver weight were similar in all groups. Food consumption was significantly increased on gestational-day 3 in the 900 ppm group but unaffected for all other time points evaluated. The calculated consumption of 2-EH, based on gestational food consumption was 0 (0 mmol/kg), 17 (0.13 mmol/kg), 59 (0.46 mmol/kg) and 191 mg/kg/day (1.49 mmol/kg), for the 0, 90, 300 and 900 ppm groups, respectively.

Exposure to dietary 2-ethylhexanol was not associated with effects on any gestational parameters. The number of corpora lutea, uterine implantation sites (live, dead, resorbed), pre- and postimplantation loss, sex ratio (%, males) and live fetal body weight per litter (all fetuses or separately by sex) were similar across all groups. No treatment-related changes in the incidence of individual, external, visceral, skeletal or total malformations or variations were observed.

In contrast, MEHP increased maternal relative liver weight at doses greater than 0.48 mmol/kg and decreased corrected wt gain at 0.97 mmol/kg. Embryo/fetal mortality was increased in all MEHP-dosed groups, with the high dos producing 78% nonlive implants/litter and 63% nonlive litters. The percent litters with malformed fetuses increased at doses greater than or equal to 0.26 mmol/kg MEHP and were 12, 26, 46, 79 and 80%, control to high dose.

In conclusion, there were no maternal or developmental toxic effects of 2-ethylhexanol dietary exposure throughout gestation at any concentration tested with doses ranging as high as 191 mg/kg/day (1.49 mmol/kg). In contrast exposure to MEHP was associated with clear developmental effects at doses as low as 0.26 mmol/kg. Thus, 2-ethoxyhexanol was not associated with developmental toxicity at dose-levels approximately 6-fold greater than the dose of MEHP that produced developmental toxicity

It was concluded by the NTP "the present study indicates that 2-EH plays essentially no role in the expression of DEHP-induced maternal and developmental toxicity."

Test substance :

2-Ethylhexanol CASNO 104-76-7 (component and surrogate)

Conclusion :
It was concluded by the NTP "the present study indicates that 2-EH plays essentially no role in the expression of DEHP-induced maternal and developmental toxicity."

Reliability : (1) valid without restriction

NTP Guideline study with data for review.

Flag : Critical study for SIDS endpoint

06.01.2004 (17) (18)

(1) MPBPWIN (v1.40) Program as found in EPIWIN v 3.05, Syracuse Research Corporation, Syracuse NY (April 2000).

(2) Sage, M; and Sage, G. Vapor Pressure. in Handbook of Property Estimation Methods for Chemicals, RS Boethling and D Mackay eds. 2000 Lewis Publishers.

(3) KOWWIN (v1.66) Program as found in EPIWIN v 3.05, Syracuse Research Corporation, Syracuse NY (April 2000).

(4) Water solubility varies for components of EP-202 from less than 1 mg/L to 6800 mg/L

(5) HYDROWIN program (v1.67) as found in EPIWIN v 3.05, Syracuse Research Corporation, Syracuse NY (April 2000).

(6) J.C. Harris in Lyman W, Reehl, W and Rosenblat, D. Handbook of Chemical Property Estimation Methods. American Chemical Society, Washingotn D.C. 1990, page 7-6

(7) EQC Level 3 Model as found in EPIWIN v 3.05, Syracuse Research Corporation, Syracuse NY (April 2000).

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(9) Hoechst AG, unveroeffentlichte Untersuchung 79.0533, (1979) zitiert im Hoechst-GDS vom 29.04.1994 as cited in IUCLID 2000 document for 2-ethylhexanal (CASNO 123-05-7).

(10) BASF AG, Oekologie-Labor; unveroeffentl. Untersuchung (1165/87)

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(12) BASF AG(1988), Labor Oekologie: Unveroeffentlichte Untersuchung: Algentest vom 16.06.1988 (2/x165/87/t72)

(13) BASF AG, Labor Oekologie; unveroeffentlichte Untersuchung, (0423/88) as cited in IUCLID 2000 document for 2-ethylhexanal (CASNO 123-05-7).

(14) BASF. Prufung der akuten oralen Toxizitat an der Ratte. Substance Oxool 740, Sub 85/420 24 Feb 1986.

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(16) Data found on NTP public database at http://ntp-apps.niehs.nih.gov/ntp_tox/index.cfm

(17) Developmental Toxicity of 2 Ethylhexanol (CAS NO. 104-76-7) in CD-1 Swiss Mice NTP Study: TER90029. Abstract available on the NTP web site and the entire report is available from NTIS.

(18) Price CJ; Tyl RW; Marr MC; Myers CB; Morrissey RE; Heindel JJ; Schwetz BA Developmental toxicity evaluation of DEHP metabolites in Swiss mice. Teratology 1991 May;43(5):457